

REMARKS

Entry of the above newly submitted claims and the following remarks are respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims. The attached pages are captioned **"Version with markings to show changes made."**

I. Amendments

The specification has been amended to correct typographical errors and inconsistencies.

Claim 39 is directed to a *microfluidics device*, as described in the specification at the cites indicated. The device, which is described generally on page 5, lines 17-31 and page 6, line 28 to page 7, line 8, comprises:

a solid substrate, as disclosed, for example, on page 32, lines 16-18 with respect to Fig. 1,

a microstructure unit, as disclosed, for example, on page 5, lines 8-10, and page 32, line 16 to page 33, line 8 with respect to Fig. 1, *having*

(i) *a sample well having an interior end surface and an exposed opening*, as disclosed, for example, on page 5, lines 4-8 and on page 9, line 15 to page 10, line 7, *and a wall surface extending therebetween*, as disclosed, for example, on page 5, lines 17-29 and page 33, lines 10-12 with respect to Fig. 1,

said sample well being adapted to receive an assay solution, as disclosed, for example, on page 2, line 30 to page 3, line 4, page 15, lines 15-19, page 4, line 31 to page 5, line 14, and page 6, lines 1-7,

(ii) *a reservoir for holding a liquid*, as disclosed, for example, on page 5, lines 8-12, and page 10, lines 8-11, *and*

(iii) *a channel extending between the reservoir and the sample well for carrying liquid in the reservoir to said sample well*, as disclosed, for example, on page 5, lines 8-12, and page 10, lines 8-11,

said sample well having at least one cross-sectional area greater than that of said channel, as disclosed, for example, on page 7, lines 23-27, and an interior border disposed within the well and spaced from said exposed opening, intermediate said opening and interior surface, as disclosed, for example, on page 5, lines 17-22, and page 42, lines 20-27 with respect to Fig. 8, wherein liquid placed in said sample well through said opening, and/or introduced therein through said channel, as disclosed, for example, at page 10, lines 27-31; page 11, lines 25-27; page 12, lines 16-21; page 13, line 12 to page 14, line 6; and page 16, lines 17-28, forms a sample volume having a meniscus created by said border, below said exposed opening, as disclosed, for example, at page 6, lines 1-8, and page 7, lines 13-29,

said sample volume being maintained substantially constant, as liquid is added to said sample volume through said opening, by liquid flow through said channel toward said reservoir, and as solvent evaporates from said sample volume, by liquid flow from said reservoir through said channel toward said sample well, as disclosed, for example, at page 5, lines 10-12 and lines 17-22, and page 11, lines 21-24.

Claim 40 adds the further limitation to the device of claim 39 that *said sample well has a cross-sectional area five to twenty times larger than the cross-sectional area of said channel, as disclosed at, for example, page 7, lines 23-27.*

Claim 41 adds the further limitation to the device of claim 39 that *said sample well has different cross-sectional areas on progressing from said interior surface to said exposed opening, as disclosed at, for example, Fig. 1 and Fig. 2.*

Claim 42 adds the further limitation to the device of claim 41 that *said sample well has a conical shape, as disclosed at, for example, Fig. 1 and Fig. 2.*

Claim 43 adds the further limitation to the device of claim 39 that *said sample well has a cylindrical shape, as disclosed at, for example, Fig. 6, Fig. 7, and Fig. 8.*

Claim 44 adds the further limitation to the device of claim 39 that *said border is a wettable/nonwettable border formed on said wall surface*, as disclosed at, for example, page 5, lines 17-31; page 6, line 28 to page 7, line 8; and page 33, lines 9-13 with respect to Fig. 1.

Claim 45 adds the further limitation to the device of claim 39 that *said border is a sharp change in the direction of the wall surface*, as disclosed at, for example, page 5, lines 17-19, and page 6, line 28 to page 7, line 8.

Claim 46 is directed to *a method of conducting a microvolume assay in an open assay zone*, as described in the specification at the cites indicated. The method, which is described generally at page 5, line 12 to page 6, line 18, and page 10, line 26 to page 11, line 24, comprises:

(a) *forming in a sample well having an exposed opening and an interior border disposed within the well and spaced from the exposed opening*, as disclosed at, for example, page 5, lines 4-8; page 9, line 15 to page 10, line 7; page 41, lines 3-5 with respect to Fig. 7B; and page 42, lines 20-27 with respect to Fig. 8B, *a sample volume having a meniscus created by said border and disposed below said opening*, as disclosed, for example, at page 6, lines 1-8, and page 7, lines 13-29,

(b) *adding liquid sample reagent to said meniscus, through said opening, and allowing the meniscus to equilibrate by liquid flow from the sample volume through a channel connecting the sample well to a reservoir*, as disclosed at, for example, page 5, lines 17-22; page 6, lines 7-10; and page 11, lines 21-24, *and*

(c) *maintaining said sample volume substantially constant, as solvent evaporates from the meniscus, by flow of solvent from the reservoir through the channel into the sample well*, as disclosed at, for example, page 5, lines 10-12.

Claim 47 adds the further limitation to the method of claim 46 that *said forming includes adding liquid from said reservoir to said well through said channel*, as disclosed at, for example, page 11, lines 25-27, page 8, lines 24-27, and page 40, lines 9-13.

Claim 48 adds the further limitation to the method of claim 46 that *said forming includes placing liquid in said well through said opening*, as disclosed at, for example, page 10, lines 27-31; page 11, lines 6-16; and page 11, lines 25-27.

Claim 49 adds the further limitation to the method of claim 46 that *said forming includes placing a liquid sample in said sample well and, following said placing, drying the liquid to deposit dry reagents within the sample well*, as disclosed at, for example, page 34, lines 11-15 with respect to Fig. 2; page 16, lines 17-18; and page 19, lines 19-21.

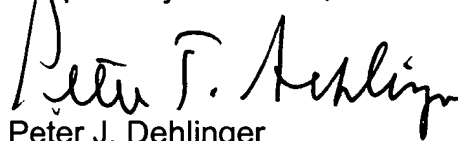
Claim 50 adds the further limitation to the method of claim 49 that *said forming includes adding solvent to dry reagents through said channel*, as disclosed at, for example, page 37, lines 17-23 with respect to Fig. 4.

No new matter has been added by these amendments.

II. Consideration of prior art

Applicant has reviewed the documents cited in the accompanying IDS 1449 form. Although certain various microfluidics devices and methods for conducting microvolume assays have been disclosed in the prior art (see the accompanying IDS 1449 form), none of the references, taken singly or in combination, discloses the combination of claimed elements, or the advantages achievable thereby.

Respectfully submitted,



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Version with Markings to Show Changes Made

This application is a continuation of Application Serial No. 09/568,786, filed May 10, 2000, now pending, which is a continuation-in-part of Application Serial [no.]No. 09/470,677, filed December 23, 1999, now pending, and claims priority to provisional applications 60/133,448, filed on May 11, 1999 and 60/140,180, filed June 18, 1999, which disclosures all of which are incorporated herein by reference.

One may also have one or a multiplicity of vertical capillary channels comprising a terminal region having a larger cross-sectional area than the capillary channel which may comprise a non-wettable region at or above the interface between the terminal region and the channel. The capillary would be placed in a reservoir to replenish liquid lost from the zone formed in the terminal region. As one added new liquid to the terminal region, initially the meniscus would be raised. Both evaporation and movement of the meniscus downward would occur, so that displacement of solution containing an active component would be minimized, keeping the volume of the zone minimal. The terminal region could be cylindrical, conical, or the like. Generally, the capillary channel would be circular, so that the terminal region would have at least about 1.2 times the diameter of the capillary channel, frequently at least about 1.5 times the diameter of the capillary channel and up to about 20 times.[.]

In many situations one may wish to [separation] separate constituents of an assay mixture. Where the substrate and product of an enzyme assay or chemical assay both provide the same signal, e.g. fluorescence, but have different mobilities, the substrate and product may be readily determined by using electrophoresis. Where multiplexed reactions are performed in the zone, one will have an interest in detecting the plurality of events that may have occurred. For example, one may have a plurality of reagents carrying electrophoretic tags (labels which have different mobilities in electrophoresis), where the result of the process in the zone is to release an electrophoretic tag in the presence of a target moiety. Where there may be a plurality of target moieties in the sample, the ability to detect the presence of the target moieties by the separation of released electrophoretic tags greatly enhances the simplicity with

which the process may be carried out. Since the entire process may be automated, the addition of the assay components, the processing of the assay, the movement of the assay components into the electrokinesis system and the separation, confusion between samples is substantially eliminated, direct comparisons are achieved between samples and controls, component handling is minimized and more accurate results can be obtained.

In Fig. 2B, liquid 220b is introduced into the wells 208b and 210b. In the present configuration, the liquid is indicated as being the same, but with different protocols the liquid could be different. The liquid 220b from the wells 208b and 210b moves by capillary action into channel 206b and halts at chamber 216b, due to the absence of capillarity at the chamber [206b] 216b. A sample may then be added to chamber 216b, which will wet the surface 218b. Where the sample is small enough, it will not contact the inlet ports 222b and 224b of channel 206b. Depending upon the nature of the solvent added to the chamber 216b and the time interval in which the solvent is allowed to stand, all or a portion of the solvent may evaporate, so that upon total evaporation, only a solvent free liquid or solid will be present.

The device has an upper plate 740 and a lower plate 742. The lower plate 742 has channels 716 and 720, which connect buffer reservoir 718 and waste reservoir 722 with zone enclosure 704, where the channel provides solution under the upper portion of the zone enclosure 712 with liquid from the channels 716 and 720. While the diameters and the reservoirs are shown as approximately equal in Fig. 7B, this is for illustration. In practice, the zone enclosure diameter would normally not be greater, usually smaller than the reservoir diameters. In this case, by having a non-wettable wall [746] 741 in the zone enclosure 708, a convex meniscus 712 is observed and the height to which the liquid in the zone can rise is restricted.